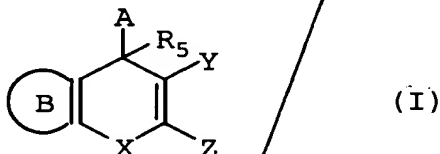


**What Is Claimed Is:**

5 *2/23* 1. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



or a pharmaceutically acceptable salt or prodrug thereof, wherein:

10 X is O or S;

Y is CN, COR<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub> or CONR<sub>x</sub>R<sub>y</sub>, wherein R<sub>7</sub>, R<sub>x</sub> and R<sub>y</sub> are independently hydrogen, C<sub>1-10</sub> alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or

15 R<sub>x</sub> and R<sub>y</sub> are taken together with the nitrogen to form a heterocycle;

Z is NR<sub>8</sub>R<sub>9</sub>, NHCOR<sub>8</sub>, N(COR<sub>8</sub>)<sub>2</sub>, N(COR<sub>8</sub>)(COR<sub>9</sub>), N=CHOR<sub>8</sub> or N=CHR<sub>8</sub>, wherein R<sub>8</sub> and R<sub>9</sub> are independently H, C<sub>1-4</sub> alkyl or aryl, or R<sub>8</sub> and R<sub>9</sub> are combined together with the group attached to them to form a heterocycle;

20 R<sub>5</sub> is hydrogen or C<sub>1-10</sub> alkyl;

A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl; and

25 B is an optionally substituted aromatic ring or an optionally substituted heteroaromatic ring.

2. The method of claim 1, with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, naphthyl, thienyl, pyridyl,

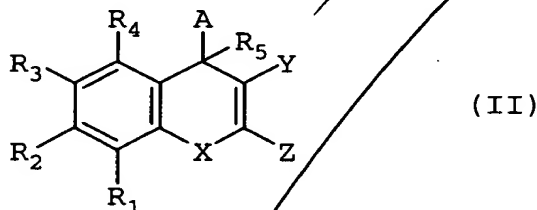
benzothienyl, quinolynyl, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen.

3. The method of claim 1, wherein B is optionally substituted and selected from the group consisting of benzo, naphtho, indolo, quino and isoquino.

4. The method of claim 1, wherein X is O.

5. The method of claim 1, wherein A is optionally substituted and selected from the group consisting of phenyl, naphthyl, quinolyl, isoquinolyl, pyridyl, thienyl, furyl, pyrrolyl, 2-phenylethyl and cyclohexyl.

6. The method of claim 1, wherein said compound has the Formula II:



or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R<sub>1</sub>-R<sub>4</sub> are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C<sub>1-10</sub> alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; or R<sub>1</sub> and R<sub>2</sub>, or R<sub>2</sub> and R<sub>3</sub>, or R<sub>3</sub> and R<sub>4</sub>, taken together with the atoms to which they are attached form an aryl, heteroaryl, partially saturated carbocyclic or partially saturated heterocyclic group, wherein said group is optionally substituted.

7. The method of claim 6, wherein A is optionally substituted and selected from the group consisting of phenyl, naphthyl, quinolyl, isoquinolyl, pyridyl, thienyl, furyl, pyrrolyl, 2-phenylethyl and cyclohexyl.

5 8. The method of claim 6, with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, naphthyl, thienyl, pyridyl, benzothienyl, quinolyl, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen.

10 9. The method of claim 6, wherein R<sub>1</sub> and R<sub>2</sub>, or R<sub>2</sub> and R<sub>3</sub>, or R<sub>3</sub> and R<sub>4</sub>, are taken together to form a structure selected from the group consisting of -O-CH<sub>2</sub>-O-, -(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>4</sub>-, -O-CH<sub>2</sub>CH<sub>2</sub>-O-, -CH<sub>2</sub>N(R)CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>N(R)CH<sub>2</sub>-, -CH<sub>2</sub>N(R)CH<sub>2</sub>CH<sub>2</sub>-, -N(R)-CH=CH-, -CH=CH-N(R)-, -O-CH=CH-, -CH=CH-O-, -S-CH=CH-, -CH=CH-S- and -N=CH-CH=N-, wherein R is hydrogen, C<sub>1-10</sub> alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

15 20 10. The method of claim 6, wherein R<sub>1</sub> and R<sub>2</sub>, or R<sub>2</sub> and R<sub>3</sub>, or R<sub>3</sub> and R<sub>4</sub>, are taken together to form a structure selected from the group consisting of -CH=CH-CH=CH-, -N=CH-CH=CH-, -CH=N-CH=CH-, -CH=CH-N=CH- and -CH=CH-CH=N-.

25 11. The method of claim 6, wherein said compound is a chromene, naphthopyran, quinopyran, isoquinopyran or indolopyran.

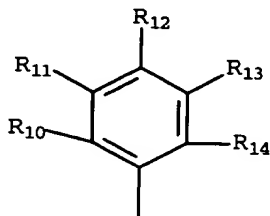
30 12. The method of claim 6, wherein X is O.

13. The method of claim 6, wherein X is O, Y is CN and Z is NH<sub>2</sub>.

14. The method of claim 6, wherein R<sub>5</sub> is hydrogen.

5 15. The method of claim 6, wherein R<sub>1</sub>-R<sub>4</sub> are independently hydrogen, halogen, hydroxy, C<sub>1-10</sub> alkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, amino, acylamido, acyloxy, alkoxy, methylenedioxy or alkylthiol.

10 16. The method of claim 6, wherein A is



15 and R<sub>10</sub>-R<sub>14</sub> are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C<sub>1-10</sub> alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; or

20 R<sub>10</sub> and R<sub>11</sub>, or R<sub>11</sub> and R<sub>12</sub>, taken together with the atoms to which they are attached form an aryl, heteroaryl, optionally substituted carbocyclic or optionally substituted heterocyclic group, wherein said group is optionally substituted.

25 17. The method of claim 16, with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans, and said compound is substituted in the 4-position of the pyran with an aryl or heteroaryl group which is phenyl, naphthyl, benzothienyl, quinolinyl, benzofuranyl or benzimidazolyl, then said

aryl or heteroaryl group is substituted at three or more positions by other than hydrogen.

18. The method of claim 16, wherein  $R_1$  and  $R_2$ , or  $R_2$  and  $R_3$ , or  $R_3$  and  $R_4$ , are taken together to form a structure selected from the group consisting of  $-\text{OCH}_2\text{O}-$ ,  $-(\text{CH}_2)_3-$ ,  $-(\text{CH}_2)_4-$ ,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2\text{CH}_2-$ ,  $-\text{N}(\text{R})-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}(\text{R})-$ ,  $-\text{O}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{O}-$ ,  $-\text{S}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{S}-$  and  $-\text{N}=\text{CH}-\text{CH}=\text{N}-$ , wherein R is hydrogen,  $\text{C}_{1-10}$  alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

19. The method of claim 16, wherein  $R_1$  and  $R_2$ , or  $R_2$  and  $R_3$ , or  $R_3$  and  $R_4$ , are taken together to form a structure selected from the group consisting of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$  and  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$ .

20. The method of claim 16, wherein  $R_{10}$  and  $R_{11}$ , or  $R_{11}$  and  $R_{12}$ , are taken together to form a structure selected from the group consisting of  $-\text{OCH}_2\text{O}-$ ,  $-(\text{CH}_2)_3-$ ,  $-(\text{CH}_2)_4-$ ,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}(\text{R})-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}(\text{R})-$ ,  $-\text{O}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{O}-$ ,  $-\text{S}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{S}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$  and  $-\text{N}=\text{CH}-\text{CH}=\text{N}-$ , wherein R is hydrogen,  $\text{C}_{1-10}$  alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

21. The method of claim 16, wherein  $R_1$  and  $R_2$  together form an optionally substituted ring, wherein said ring is selected from the group consisting of benzo, pyrido, furo, thieno, pyrrolo, imidazolo and pyrazo.

22 The method of claim 21, with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans, and said compound is substituted in the 4-position of the pyran with an aryl or heteroaryl group which is phenyl, naphthyl, benzothienyl, quinoliny, benzofuranyl or benzimidazolyl then said aryl or heteroaryl group is substituted at three or more positions by other than hydrogen.

23. The method of claim 21, wherein said compound is naphthopyran, quinopyran, isoquinopyran or indolopyran.

24. The method of claim 21, wherein  $R_{10}$  and  $R_{11}$ , or  $R_{11}$  and  $R_{12}$ , are taken together to form a structure selected from the group consisting of  $-\text{OCH}_2\text{O}-$ ,  $-(\text{CH}_2)_3-$ ,  $-(\text{CH}_2)_4-$ ,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}(\text{R})-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}(\text{R})-$ ,  $-\text{O}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{O}-$ ,  $-\text{S}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{S}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$  and  $-\text{N}=\text{CH}-\text{CH}=\text{N}-$ , wherein R is hydrogen,  $\text{C}_{1-10}$  alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

25. The method of claim 21, wherein  $R_3$ ,  $R_4$  and  $R_5$  are each hydrogen.

26. The method of claim 1, wherein said compound is selected from the group consisting of:

2-Amino-3-cyano-7-dimethylamino-4-(3-methoxy-4,5-methylene-  
dioxyphe~~nyl~~)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-  
4*H*-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(1-naphthyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-naphthyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4-methoxyphenyl)-  
4*H*-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,6-dimethoxy-  
phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-trifluoromethylphenyl)-4*H*-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylphenyl)-4*H*-  
chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4-fluorophenyl)-4*H*-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4,5-trimethoxyphenyl)-4*H*-  
chromene;

20 2-Acetamido-3-cyano-7-dimethylamino-4-(3,4-methylenedioxy-  
phenyl)-4*H*-chromene;

2-Di(ethoxycarbonyl)amino-3-cyano-7-dimethylamino-4-(3,4-  
methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-4,5-methylenedioxy-  
phenyl)-4*H*-chromene;

25 2-Amino-3-cyano-7-diethylamino-4-(3-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-methyl-3-nitrophenyl)-4*H*-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethylphenyl)-4*H*-  
chromene;

30 3-Cyano-7-dimethylamino-4-(4,5-methylenedioxyphenyl)-2-  
propionamido-4*H*-chromene;

00905840 " 110600

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-methoxyphenyl)-4*H*-chromene;

5 2-Amino-3-cyano-7-diethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenyl-4*H*-chromene;

2-Benzylidenamino-3-cyano-7-dimethylamino-4-phenyl-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-cyclohexyl-4*H*-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-3-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,4,5-trifluorophenyl)-4*H*-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(2,3,4-trifluorophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-3-nitrophenyl)-4*H*-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-ethylenedioxyphenyl)-4*H*-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-fluoro-3-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-pyridyl)-4*H*-chromene;

30 2-Amino-3-cyano-6,7-methylenedioxy-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

09705840-110600



2-Amino-3-cyano-7-ethylamino-4-(3-methoxy-4,5-methylenedioxy-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-trifluoromethyl-phenyl)-4*H*-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-4-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoromethylenedioxy-phenyl)-4*H*-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoro-5-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-furyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-thienyl)-4*H*-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-6-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-nitrophenyl)-4*H*-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3-phenoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-phenylethyl)-4*H*-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-5-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3-difluoro-4-trifluoromethyl-phenyl)-4*H*-chromene;

30 2,7-Diamino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-pyridyl)-4*H*-chromene;

009071 04850760

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-(4-methoxyphenoxy)phenyl)-4*H*-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3,5-dichlorophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-quinolyl)-4*H*-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(2-quinolyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenylmethyl-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-carboxaldehydephenyl)-4*H*-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(4-bromo-3,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-7-acetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

2,7-Diamino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

20 2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-6,7,8,9,10,11-hexahydro-4*H*-pyrido[3,2,1-ij]quino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-indolo[4,5-b]pyran;

25 2-Amino-3-cyano-7-ethylamino-6-methyl-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2,7-Diamino-3-cyano-8-methyl-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-7-chloroacetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

30 2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4*H*-indolo[4,5-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromophenyl)-4*H*-chromene;

00907T"04850460

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dibromophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyanophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chlorophenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-difluorophenyl)-4H-chromene;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-bis(trifluoromethyl)phenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-5-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(4-bromo-3,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloromethylphenyl)-4H-chromene;

00907T 04850260

2-Amino-3-cyano-7-dimethylamino-4-(3-chloromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyano-4-fluorophenyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3-nitro-4-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

10 2-Amino-3-cyano-7-methoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylthiophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluorophenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(3-difluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-hydroxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethoxyphenyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3-methylaminophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-dimethylaminophenyl)-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(3-iodo-4,5-dimethoxyphenyl)-4H-naptho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3-indo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-naptho[1,2-b]pyran;

00907 " 04850260

2-Amino-3-cyano-7-dimethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-4,5-dimethoxyphenyl)-4H-chromene;

5 2-Chloroacetamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Acrylamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

10 3-Cyano-7-dimethylamino-2-succinimido-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

3-Cyano-7-dimethylamino-2-phenylureido-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran;

15 2-Amino-3-cyano-7-dimethylamino-4-(5-bromo-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-3-pyridyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-2-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-naphtho[2,1-b]pyran;

25 2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-2-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quinol[5,6-b]pyran;

30 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-isoquinol[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quinol[8,7-b]pyran;

00907T 04850260

2-Amino-3-cyano-7-ethoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8,9,10-tetrahydro-4H-naphtho[1,2-b]pyran;

5 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8-dimethyl-4H-chromene;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-quinol[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-4H-naphtho[1,2-b]pyran;

10 2-Amino-6-chloro-3-cyano-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-methoxy-4-(3,4,5-trimethoxyphenyl)-4H-chromene;

15 2-Amino-3-cyano-7-methoxy-4-(3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-cyanophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-chlorophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-bromophenyl)-4H-chromene;

20 2-Amino-3-cyano-7-methoxy-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methoxy-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methylthio-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-chloro-3-pyridyl)-4H-chromene;

25 2-Amino-3-cyano-7-methoxy-4-(5-bromo-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methyl-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-chloro-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

30 2-Amino-3-cyano-7-bromo-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-bromo-4-(5-methyl-3-pyridyl)-4H-chromene;

00907 04850 60

2-Amino-3-cyano-7-chloro-4-(5-methyl-3-pyridyl)-4H-chromene;  
2-Amino-3-cyano-7-ethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-  
4H-chromene;  
2-Amino-3-cyano-7-ethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;  
and  
2-Amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
chromene.

27. The method of claim 1, wherein said disorder is cancer.

28. The method of claim 27, wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, malignant melanoma, choriocarcinoma, mycosis fungoides, head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma.

29. The method of claim 27, with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isquinopyrans and A is phenyl, naphthyl, thienyl, pyridyl, benzothienyl, quinolinyl, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen.

30. The method of claim 27, wherein said cancer is a drug resistant cancer.

5 31. The method of claim 30, with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, naphthyl, thienyl, pyridyl, benzothienyl, quinoliny, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen.

10 32. The method of claim 27 or 30, additionally comprising administering at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent.

15 33. The method of claim 32, wherein said known cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin, Rituxan and alanosine.

20 34. The method of claim 27 or 30, additionally comprising treating with radiation-therapy.

25



35. The method of claim 27 or 30, wherein said compound is administered after surgical treatment for cancer.

36. The method of claim 1, wherein said disorder is an autoimmune disease.

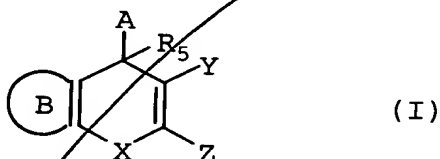
37. The method of claim 1, wherein said disorder is rheumatoid arthritis.

38. The method of claim 1, wherein said disorder is inflammation or inflammatory bowel disease.

39. The method of claim 1, wherein said disorder is psoriasis.

40. The method of claim 1, wherein said disorder is a skin disease.

41. A pharmaceutical composition comprising a pharmaceutically acceptable excipient or carrier and a compound of Formula I:



or a pharmaceutically acceptable salt or prodrug thereof, wherein:

X is O or S;

Y is CN, COR<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub> or CONR<sub>x</sub>R<sub>y</sub>, wherein R<sub>7</sub>, R<sub>x</sub> and R<sub>y</sub> are independently hydrogen, C<sub>1-10</sub> alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R<sub>x</sub> and R<sub>y</sub> are taken together with the nitrogen to which they are attached to form a heterocycle;

Z is  $\text{NR}_8\text{R}_9$ ,  $\text{NHCOR}_8$ ,  $\text{N}(\text{COR}_8)_2$ ,  $\text{N}(\text{COR}_8)(\text{COR}_9)$ ,  $\text{N}=\text{CHOR}_8$  or  $\text{N}=\text{CHR}_8$ , wherein  $\text{R}_8$  and  $\text{R}_9$  are independently H,  $\text{C}_{1-4}$  alkyl or aryl, or  $\text{R}_8$  and  $\text{R}_9$  are combined together with the group attached to them to form a heterocycle;

$\text{R}_5$  is hydrogen or  $\text{C}_{1-10}$  alkyl;

A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl; and

B is an optionally substituted aromatic ring or an optionally substituted heteroaromatic ring;

with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, naphthyl, thienyl, pyridyl, benzothienyl, quinoliny, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen.

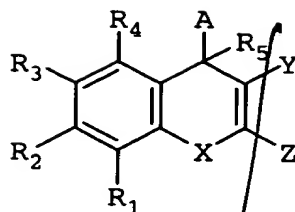
~~42. The pharmaceutical composition of claim 41, wherein B is optionally substituted and selected from the group consisting of benzo, naphtho, indolo, quino and isoquino and A is optionally substituted and selected from the group consisting of phenyl, naphthyl, pyridyl, quinolyl, isquinolyl, thienyl, furyl, pyrrolyl, 2-phenylethyl and cyclohexyl.~~

~~43. The pharmaceutical composition of claim 41, wherein X is O.~~

44. The pharmaceutical composition of claim 41, wherein X is O, Y is CN and Z is  $\text{NH}_2$ .

45. The pharmaceutical composition of claim 41, wherein  $\text{R}_5$  is hydrogen.

46. The pharmaceutical composition of claim 41, comprising a pharmaceutically acceptable excipient or carrier and a compound of Formula II:



(II)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

$R_1$ - $R_4$  are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group,  $C_{1-10}$  alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; or

$R_1$  and  $R_2$ , or  $R_2$  and  $R_3$ , or  $R_3$  and  $R_4$ , taken together with the atoms to which they are attached form an aryl, heteroaryl, partially saturated carbocyclic or partially saturated heterocyclic group, wherein said group is optionally substituted;

X is O or S;

Y is CN,  $COR_7$ ,  $CO_2R_7$  or  $CONR_xR_y$ , wherein  $R_7$ ,  $R_x$  and  $R_y$  are independently hydrogen,  $C_{1-10}$  alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or  $R_x$  and  $R_y$

are taken together with the nitrogen to which they are attached to form a heterocycle;

Z is  $NR_8R_9$ ,  $NHCOR_8$ ,  $N(COR_8)_2$ ,  $N(COR_8)(COR_9)$ ,  $N=CHOR_8$  or  $N=CHR_8$ , wherein  $R_8$  and  $R_9$  are independently H,  $C_{1-4}$  alkyl or aryl, or  $R_8$  and  $R_9$  are combined together with the group attached to them to form a heterocycle;

$R_5$  is hydrogen or  $C_{1-10}$  alkyl; and

A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl;

00907 045040 110600

with the proviso that when said compound is selected from the group consisting of 4H-naphthopyrans, 4H-quinopyrans and 4H-isoquinopyrans and A is phenyl, naphthyl, thienyl, pyridyl, benzothienyl, quinolinyl, benzofuranyl or benzimidazolyl, then A is substituted at three or more positions by other than hydrogen.

47. The pharmaceutical composition of claim 46, wherein  $R_1$  and  $R_2$ , or  $R_2$  and  $R_3$ , or  $R_3$  and  $R_4$ , are taken together to form a structure selected from the group consisting of  $-\text{OCH}_2\text{O}-$ ,  $-(\text{CH}_2)_3-$ ,  $-(\text{CH}_2)_4-$ ,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2\text{CH}_2-$ ,  $-\text{N}(\text{R})-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}(\text{R})-$ ,  $-\text{O}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{O}-$ ,  $-\text{S}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{S}-$  and  $-\text{N}=\text{CH}-\text{CH}=\text{N}-$ , wherein R is hydrogen,  $\text{C}_{1-10}$  alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

48. The pharmaceutical composition of claim 46, wherein  $R_1$  and  $R_2$ , or  $R_2$  and  $R_3$ , or  $R_3$  and  $R_4$ , are taken together to form a structure selected from the group consisting of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$  and  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$ .

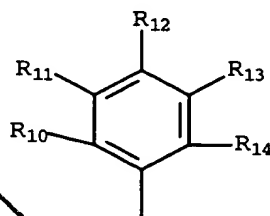
49. The pharmaceutical composition of claim 46, wherein X is O.

50. The pharmaceutical composition of claim 46, wherein X is O, Y is CN and Z is  $\text{NH}_2$ .

51. The pharmaceutical composition of claim 46, wherein  $R_5$  is hydrogen.

52. The pharmaceutical composition of claim 46, wherein R<sub>1</sub>-R<sub>4</sub> are independently hydrogen, halogen, hydroxy, C<sub>1-10</sub> alkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, amino, acylamido, acyloxy, alkoxy, methylenedioxy or alkylthiol.

53. The pharmaceutical composition of claim 46 comprising said compound or a pharmaceutically acceptable salt or prodrug thereof, wherein A is



and R<sub>10</sub>-R<sub>14</sub> are independently hydrogen, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C<sub>1-10</sub> alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthiol; or

R<sub>10</sub> and R<sub>11</sub>, or R<sub>11</sub> and R<sub>12</sub>, taken together with the atoms to which they are attached form an aryl, heteroaryl, optionally substituted carbocyclic or optionally substituted heterocyclic group, wherein said group is optionally substituted.

54. The pharmaceutical composition of claim 53, wherein R<sub>1</sub> and R<sub>2</sub>, or R<sub>2</sub> and R<sub>3</sub>, or R<sub>3</sub> and R<sub>4</sub>, are taken together to form a structure selected from the group consisting of -OCH<sub>2</sub>O-, -(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>4</sub>-, -OCH<sub>2</sub>CH<sub>2</sub>O-, -CH<sub>2</sub>N(R)CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>N(R)CH<sub>2</sub>-, -CH<sub>2</sub>N(R)CH<sub>2</sub>CH<sub>2</sub>-, -N(R)-CH=CH-, -CH=CH-N(R)-, -O-CH=CH-, -CH=CH-O-, -S-CH=CH-, -CH=CH-S- and -N=CH-CH=N-, wherein R is hydrogen, C<sub>1-10</sub> alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a

heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

5            55. The pharmaceutical composition of claim 53, wherein  $R_1$  and  $R_2$ , or  $R_2$  and  $R_3$ , or  $R_3$  and  $R_4$ , are taken together to form a structure selected from the group consisting of  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$  and  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$ .

10            56. The pharmaceutical composition of claim 53, wherein  $R_{10}$  and  $R_{11}$ , or  $R_{11}$  and  $R_{12}$ , are taken together to form a structure selected from the group consisting of  $-\text{OCH}_2\text{O}-$ ,  $-(\text{CH}_2)_3-$ ,  $-(\text{CH}_2)_4-$ ,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}(\text{R})-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}(\text{R})-$ ,  $-\text{O}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{O}-$ ,  $-\text{S}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{S}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$  and  $-\text{N}=\text{CH}-\text{CH}=\text{N}-$ , wherein R is hydrogen,  $\text{C}_{1-10}$  alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl.

15

20

25            57. The pharmaceutical composition of claim 53, wherein  $R_1$  and  $R_2$  together form an optionally substituted ring, wherein said ring is selected from the group consisting of benzo, pyrido, furo, thieno, pyrrolo, imidazo and pyrazo.

30            58. The pharmaceutical composition of claim 57, wherein said ring is selected from the group consisting of benzo, pyrido and pyrrolo.

59. The pharmaceutical composition of claim 57, wherein  $R_{10}$  and  $R_{11}$ , or  $R_{11}$  and  $R_{12}$ , are taken together to form a structure selected from the

group consisting of  $-\text{OCH}_2\text{O}-$ ,  $-(\text{CH}_2)_3-$ ,  $-(\text{CH}_2)_4-$ ,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ,  
 $-\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{N}(\text{R})\text{CH}_2-$ ,  $-\text{CH}_2\text{N}(\text{R})\text{CH}_2\text{CH}_2-$ ,  
 $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$ ,  $-\text{N}(\text{R})-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}(\text{R})-$ ,  $-\text{O}-\text{CH}=\text{CH}-$ ,  
 $-\text{CH}=\text{CH}-\text{O}-$ ,  $-\text{S}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{S}-$ ,  $-\text{N}=\text{CH}-\text{CH}=\text{CH}-$ ,  
5  $-\text{CH}=\text{N}-\text{CH}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{N}=\text{CH}-$ ,  $-\text{CH}=\text{CH}-\text{CH}=\text{N}-$  and  
 $-\text{N}=\text{CH}-\text{CH}=\text{N}-$ , wherein R is hydrogen,  $\text{C}_{1-10}$  alkyl, haloalkyl, aryl, fused  
aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl,  
arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl,  
heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or  
10 aminoalkyl.

60. The pharmaceutical composition of claim 57, wherein  $\text{R}_3$ ,  $\text{R}_4$   
and  $\text{R}_5$  are each hydrogen.

61. The pharmaceutical composition of claim 46, wherein said  
compound is selected from the group consisting of:

2-Amino-3-cyano-7-dimethylamino-4-(3-methoxy-4,5-methylene-  
dioxyphe~~nyl~~)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphe~~nyl~~)-  
4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(1-naphthyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-naphthyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4-methoxyphenyl)-  
4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,6-dimethoxy-  
phenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-trifluoromethylphenyl)-4H-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylphenyl)-4H-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4-fluorophenyl)-4H-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4,5-trimethoxyphenyl)-4H-chromene;

2-Acetamido-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4H-chromene;

5 2-Di(ethoxycarbonyl)amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-diethylamino-4-(3-pyridyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(4-methyl-3-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethylphenyl)-4H-chromene;

15 3-Cyano-7-dimethylamino-4-(4,5-methylenedioxyphenyl)-2-propionamido-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-methoxyphenyl)-4H-chromene;

20 2-Amino-3-cyano-7-diethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenyl-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-cyclohexyl-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-3-trifluoromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,4,5-trifluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3,4-trifluorophenyl)-4H-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-nitrophenyl)-4H-chromene;

009077 04850260



2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-3-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-ethylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethoxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-fluoro-3-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-ethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-4-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoromethylenedioxyphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-furyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-thienyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-trifluoromethylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-6-nitrophenyl)-4*H*-chromene;

009077 04850260

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-phenoxyphenyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(2-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-phenylethyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-nitrophenyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-5-trifluoromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3-difluoro-4-trifluoromethylphenyl)-4H-chromene;

2,7-Diamino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(4-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-(4-methoxyphenoxy)phenyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3,5-dichlorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-trifluoromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-quinolyl)-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(2-quinolyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenylmethyl-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-carboxaldehydephenyl)-4H-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(4-bromo-3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-7-acetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

009071" 04850260

2,7-Diamino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-ethylamino-6-methyl-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

5 2,7-Diamino-3-cyano-8-methyl-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-7-chloroacetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromophenyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(3,5-dibromophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyanophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chlorophenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(3-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-difluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-bis(trifluoromethyl)-phenyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-5-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloromethylphenyl)-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(3-chloromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyano-4-fluorophenyl)-4H-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(3-nitro-4-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylthiophenyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-difluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-hydroxyphenyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylaminophenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(3-dimethylaminophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-iodo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-4,5-dimethoxyphenyl)-4H-chromene;

25 2-Chloroacetamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Acrylamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

3-Cyano-7-dimethylamino-2-succinimido-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

30 3-Cyano-7-dimethylamino-2-phenylureido-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

009077 " 04850260

2-Amino-3-cyano-7-dimethylamino-4-(5-bromo-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-3-pyridyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-2-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-2-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-ethoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8-dimethyl-4H-chromene;

15 2-Amino-3-cyano-7-methoxy-4-(3,4,5-trimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-cyanophenyl)-4H-chromene;

20 2-Amino-3-cyano-7-methoxy-4-(3-chlorophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-bromophenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-methoxy-3-pyridyl)-4H-chromene;

25 2-Amino-3-cyano-7-methoxy-4-(5-methylthio-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-chloro-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(5-bromo-3-pyridyl)-4H-chromene;

30 2-Amino-3-cyano-7-methyl-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-chloro-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

009071 04850260

2-Amino-3-cyano-7-bromo-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-bromo-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-chloro-4-(5-methyl-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-ethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-ethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;  
and

2-Amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene.

62. The pharmaceutical composition of claim 57, wherein said compound is selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-6,7,8,9,10,11-hexahydro-4H-pyrido[3,2,1-ij]quino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(4-bromo-3,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3-iodo-4,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-naphtho[2,1-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
isoquino[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
quino[8,7-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-4H-  
naphtho[1,2-b]pyran;

2-Amino-6-chloro-3-cyano-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-  
4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8,9,10-  
tetrahydro-4H-naphtho[1,2-b]pyran; and

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-quino[5,6-b]pyran.

63. The pharmaceutical composition of claim 57, wherein said  
compound is selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-  
indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4H-  
indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-  
indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran;

and

9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
indolo[4,5-b]pyran.

64. The pharmaceutical composition of claim 41, further comprising at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent.

5  
65. The pharmaceutical composition of claim 64, wherein said known cancer chemotherapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 10 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguanzone, epirubicin, aclarubicin, bleomycin, mitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin, Rituxan and alanosine.

15 66. The pharmaceutical composition of claim 41, wherein said excipient or carrier is selected from the group consisting of saccharides, starch pastes, gelatin, tragacanth, cellulose preparations, calcium phosphates and polyvinyl pyrrolidone.

20 67. The pharmaceutical composition of claim 66, wherein said excipient or carrier is a saccharide selected from the group consisting of lactose, sucrose, manitol and sorbitol.

25 68. The pharmaceutical composition of claim 41, wherein said excipient or carrier is a lipophilic solvent.

30 69. The pharmaceutical composition of claim 68, wherein said lipophilic solvent is selected from the group consisting of fatty oils, fatty acid esters, polyethylene glycols and paraffin hydrocarbons.

09705840 "110600



70. The pharmaceutical composition of claim 69, wherein said lipophilic solvent is selected from the group consisting of sesame oil, ethyl oleate, triglycerides, polyethylene glycol-400, cremophor and cyclodextrins.

5 71. The pharmaceutical composition of claim 41, wherein said excipient or carrier is selected from the group consisting of vegetable oils, mineral oils, white petrolatum, branched chain fats, branched chain oils, animal fats and high molecular weight alcohol (greater than C<sub>12</sub>).

10 72. The pharmaceutical composition of claim 41, wherein said excipient or carrier is a saline solution.

73. A chromene, selected from the group consisting of:

15 2-Amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-naphthyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4,5-trimethoxyphenyl)-4H-chromene;

20 2-Acetamido-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4H-chromene;

2-Di(ethoxycarbonyl)amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-4,5-methylenedioxyphenyl)-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(4-methyl-3-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethylphenyl)-4H-chromene;

30 3-Cyano-7-dimethylamino-4-(4,5-methylenedioxyphenyl)-2-propionamido-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-diethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-phenyl-4H-chromene;

2-Benzylidenamino-3-cyano-7-dimethylamino-4-phenyl-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-cyclohexyl-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-3-trifluoromethylphenyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(2,4,5-trifluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3,4-trifluorophenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-3-nitrophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-nitrophenyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-ethylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-dimethoxyphenyl)-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(4-fluoro-3-trifluoromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-pyridyl)-4H-chromene;

2-Amino-3-cyano-6,7-methylenedioxy-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

30 2-Amino-3-cyano-7-ethylamino-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-chromene;

00905840 110600

2-Amino-3-cyano-7-dimethylamino-4-(2-fluoro-5-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-4-trifluoromethyl-phenyl)-4*H*-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoromethylenedioxy-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,4-difluoro-5-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-furyl)-4*H*-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(5-nitro-2-thienyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-trifluoromethyl-phenyl)-4*H*-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-6-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-chloro-5-nitrophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-phenoxyphenyl)-4*H*-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(2-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-phenylethyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-nitrophenyl)-4*H*-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-5-trifluoromethyl-phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2,3-difluoro-4-trifluoromethyl-phenyl)-4*H*-chromene;

2,7-Diamino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4*H*-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(4-pyridyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dimethoxyphenyl)-4*H*-chromene;

09705840-110600

2-Amino-3-cyano-7-dimethylamino-4-(3-(4-methoxyphenoxy)phenyl)-  
4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-dichlorophenyl)-4*H*-  
chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3-fluoro-6-trifluoromethyl-  
phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-quinolyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-quinolyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-phenylmethyl-4*H*-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(4-carboxaldehydephenyl)-4*H*-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-bromo-3,5-dimethoxy-  
phenyl)-4*H*-chromene;

15 2-Amino-7-acetamido-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-  
chromene;

2,7-Diamino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-  
chromene;

2-Amino-3-cyano-7-ethylamino-6-methyl-4-(3-methoxy-4,5-  
methylenedioxyphenyl)-4*H*-chromene;

20 2,7-Diamino-3-cyano-8-methyl-4-(3-methoxy-4,5-methylenedioxy-  
phenyl)-4*H*-chromene;

2-Amino-7-chloroacetamido-3-cyano-4-(3-bromo-4,5-dimethoxy-  
phenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-bromophenyl)-4*H*-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(3,5-dibromophenyl)-4*H*-  
chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyanophenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylphenyl)-4*H*-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-chlorophenyl)-4*H*-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(3-methoxyphenyl)-4*H*-  
chromene;

009077" 04850250

2-Amino-3-cyano-7-dimethylamino-4-(3,5-difluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3,5-bis(trifluoromethyl)phenyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-5-methoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloromethylphenyl)-4H-chromene;

10 2-Amino-3-cyano-7-dimethylamino-4-(3-chloromethylphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-cyano-4-fluorophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-nitro-4-fluorophenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(3-bromo-4,5-methylenedioxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethylthiophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-difluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-hydroxyphenyl)-4H-chromene;

25 2-Amino-3-cyano-7-dimethylamino-4-(3-trifluoromethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-methylaminophenyl)-4H-chromene;

30 2-Amino-3-cyano-7-dimethylamino-4-(3-dimethylaminophenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(3-iodo-4,5-dimethoxyphenyl)-4H-chromene;

009077" 04350260

2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxy-phenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;

5 2-Amino-3-cyano-7-dimethylamino-4-(3-chloro-4,5-dimethoxy-phenyl)-4H-chromene;

2-Chloroacetamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

10 2-Acrylamido-3-cyano-7-dimethylamino-4-(3-bromo-4,5-dimethoxy-phenyl)-4H-chromene;

3-Cyano-7-dimethylamino-2-succinimido-4-(3-bromo-4,5-dimethoxy-phenyl)-4H-chromene;

3-Cyano-7-dimethylamino-2-phenylureido-4-(3-bromo-4,5-dimethoxy-phenyl)-4H-chromene;

15 2-Amino-3-cyano-7-dimethylamino-4-(5-bromo-3-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-3-pyridyl)-4H-chromene;

20 2-Amino-3-cyano-7-dimethylamino-4-(6-methyl-2-pyridyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(2-bromo-4,5-methylenedioxy-phenyl)-4H-chromene;

2-Amino-3-cyano-7-dimethylamino-4-(4-chloro-2-nitrophenyl)-4H-chromene;

25 2-Amino-3-cyano-7-ethoxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8-dimethyl-4H-chromene;

30 2-Amino-3-cyano-7-methoxy-4-(3,4,5-trimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3,5-dimethoxyphenyl)-4H-chromene;

2-Amino-3-cyano-7-methoxy-4-(3-methoxyphenyl)-4H-chromene;

00907 04850260

2-Amino-3-cyano-7-methoxy-4-(3-cyanophenyl)-4H-chromene;  
2-Amino-3-cyano-7-methoxy-4-(3-chlorophenyl)-4H-chromene;  
2-Amino-3-cyano-7-methoxy-4-(3-nitrophenyl)-4H-chromene;  
2-Amino-3-cyano-7-methoxy-4-(3-bromophenyl)-4H-chromene;  
5 2-Amino-3-cyano-7-methoxy-4-(5-methyl-3-pyridyl)-4H-chromene;  
2-Amino-3-cyano-7-methoxy-4-(5-methoxy-3-pyridyl)-4H-chromene;  
2-Amino-3-cyano-7-methoxy-4-(5-methylthio-3-pyridyl)-4H-  
chromene;  
2-Amino-3-cyano-7-methoxy-4-(5-chloro-3-pyridyl)-4H-chromene;  
10 2-Amino-3-cyano-7-methoxy-4-(5-bromo-3-pyridyl)-4H-chromene;  
2-Amino-3-cyano-7-methyl-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
chromene;  
2-Amino-3-cyano-7-chloro-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
chromene;  
15 2-Amino-3-cyano-7-bromo-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
chromene;  
2-Amino-3-cyano-7-bromo-4-(5-methyl-3-pyridyl)-4H-chromene;  
2-Amino-3-cyano-7-chloro-4-(5-methyl-3-pyridyl)-4H-chromene;  
2-Amino-3-cyano-7-ethylamino-4-(3-bromo-4,5-dimethoxyphenyl)-  
20 4H-chromene;  
2-Amino-3-cyano-7-ethylamino-4-(5-methyl-3-pyridyl)-4H-chromene;  
and  
2-Amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
chromene.

25 74. A naphthopyran, quinopyran or isoquinopyran, selected from  
the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-  
6,7,8,9,10,11-hexahydro-4H-pyrido[3,2,1-ij]quino[5,6-b]pyran;  
30 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-  
naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(4-bromo-3,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-naphtho[1,2-b]pyran;

5 2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-7-dimethylamino-4-(3-iodo-4,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

10 2-Amino-3-cyano-7-dimethylamino-4-(4-acetoxy-3,5-dimethoxyphenyl)-4H-naphtho[1,2-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-naphtho[2,1-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quinol[5,6-b]pyran;

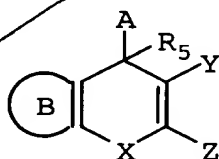
15 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-isoquinol[5,6-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-quinol[8,7-b]pyran;

20 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7,8,9,10-tetrahydro-4H-naphtho[1,2-b]pyran; and

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-quinol[5,6-b]pyran.

75. An indolopyran of Formula I:



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

B is optionally substituted indolo;

X is O;



Y is CN, COR<sub>7</sub>, CO<sub>2</sub>R<sub>7</sub> or CONR<sub>x</sub>R<sub>y</sub>, wherein R<sub>7</sub>, R<sub>x</sub> and R<sub>y</sub> are independently hydrogen, C<sub>1-10</sub> alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R<sub>x</sub> and R<sub>y</sub> are taken together with the nitrogen to which they are attached to form a heterocycle;

Z is NR<sub>8</sub>R<sub>9</sub>, NHCOR<sub>8</sub>, N(COR<sub>8</sub>)<sub>2</sub>, N(COR<sub>8</sub>)(COR<sub>9</sub>), N=CHOR<sub>8</sub> or N=CHR<sub>8</sub>, wherein R<sub>8</sub> and R<sub>9</sub> are independently H, C<sub>1-4</sub> alkyl or aryl, or R<sub>8</sub> and R<sub>9</sub> are combined together with the group attached to them to form a heterocycle;

R<sub>5</sub> is hydrogen or C<sub>1-10</sub> alkyl; and

A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl.

76. The compound of claim 75, wherein said compound is an optionally substituted 4H-indolo[4,5-b]pyran.

77. The compound of claim 76, wherein A is optionally substituted phenyl.

78. The compound of claim 77, wherein said compound is selected from the group consisting of:

2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-indolo[4,5-b]pyran;

2-Amino-3-cyano-4-(3-nitrophenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3-cyanophenyl)-4*H*-indolo[4,5-*b*]pyran;

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4*H*-indolo[4,5-*b*]pyran;

and

5      9-Acetamide-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4*H*-  
indolo[4,5-*b*]pyran.

add  
B17

add  
C8

add  
D5

009077" 04850260